REMARKS

The Office Action dated January 7, 2003 presents the examination of claims 3-5, 7-8, 19, 21, and 32-34. Pending claims 6, 9-18, 20, and 22-31 are withdrawn from consideration. Claims 19, 32, and 33 are amended. No new matter is inserted into the application.

Specification

The Examiner objects to the specification for containing hyperlinks. Applicants amend the specification to delete the hyperlinks. Thus, the instant objection is overcome.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejects claims 3-5, 7-8, 19, 21, and 23-24 under 35 U.S.C. § 112, second paragraph for allegedly being indefinite. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Claim 32

The Examiner asserts that to which polypeptide the "polypeptide" in the last paragraph of claim 32 refers is not clear. Applicants amend the claim to recite "polypeptide of (a)

and (b)…." Thus, the instant rejection is overcome.

Claim 19

The Examiner asserts that the "protein" of claim 19 is unclear. Claim 19 is amended to make clear that the "protein" is that which is encoded by the polynucleotide of claim 32, or that which is produced by the process of claim 5. Thus, the instant rejection is overcome.

Claim 33

The Examiner rejects claim 33 for reciting "at least one of the nucleic acids of claim 19" because claim 19 does not provide antecedent basis for "one of the nucleic acids." Claim 33 is amended to delete the phrase "at least one of the nucleic acids." The claim now refers to the "polynucleotide" of claim 19. Thus, the instant rejection is overcome.

Rejection under 35 U.S.C. § 112, first paragraph

Written Description

The Examiner rejects claims 3-5, 7-8, 19, 21, and 32-34 under 35 U.S.C. § 112, first paragraph for an alleged lack of written description. Applicants respectfully traverse. Reconsideration

of the claims and withdrawal of the instant rejection are respectfully requested.

On page 4 of the Office Action, the Examiner acknowledges that the amino acid sequence of SEQ ID NO:2 and the polynucleotide of SEQ ID NO:1 are adequately described in the specification. Independent claim 32 is amended to recite an isolated polynucleotide selected from the group consisting of: (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1, and (b) a polynucleotide comprising the nucleotide sequence from nucleotide 12 to nucleotide 2900 of SEQ ID NO:1. The nucleotide sequence from nucleotide 12 to nucleotide 2900 of SEQ ID NO:1 is described as CDS (Coding Sequence) in SEQ ID NO:1, and corresponds to the coding sequence of the amino acid sequence of SEQ ID NO:2.

Applicants respectfully submit that the claimed polynucleotides are adequately described in the specification, such that the requirements of 35 U.S.C. § 112, first paragraph, written description are met. Withdrawal of the instant rejection is therefore respectfully requested.

Enablement

The Examiner also rejects claims 3-5, 7-8, 19, 21, and 32-34 under 35 U.S.C. § 112, first paragraph for allegedly not being

enabled by the specification. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

The Examiner asserts that the specification does not teach how to use the claimed invention. Specifically, the Examiner asserts that the specification does not teach the intended use of the polynucleotides for treatment and prevention of tumors. Applicants respectfully disagree. Example 2, on pages 47-48 of the specification, shows that the transfection of VA-13 cells with the polynucleotide encoding SART-3 activates CTLs and produces IFN-γ. These results demonstrate that SART-3 should be useful in the treatment of cancer.

The Examiner relies on, for example, Ezzell (1995) and Spitler (1995) to assert that cancer vaccines may not work. In repudiation thereof, Applicants submit herewith the journal article of Miyagi et al., *Clinical Cancer Research*, 7:3950-3962 (2001), which was published by Dr. Itoh after the filing date of the present application (see Exhibit 1). The article describes the results of a clinical test wherein peptides derived from SART-3 were administered to cancer patients. The article reports that the administration of SART-3 peptides induced immunization against cancer in the patients. Again, these results demonstrate that

SART-3 should be useful in cancer vaccination.

Taking into account Dr. Itoh's publication and the disclosure of the present application, it is clear that the instant claims are enabled, such that the requirements under 35 U.S.C. § 112, first paragraph, enablement, are met. Withdrawal of the instant rejection is therefore respectfully requested.

Rejection under 35 U.S.C. § 102(b)

The Examiner rejects claims 7-8, 19, 21, 23, and 33 under 35 U.S.C. § 102(b) for allegedly being anticipated by Nagase et al. (*DNA Research*, 2:167-174, 1995). Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Nagase et al. discloses the sequence of KIAA0156. As described on page 49, lines 3-7 of the specification, the nucleotide sequence of SART-3 is different from the nucleotide sequence of KIAA0156 by one nucleotide. Thus, Nagase et al. fails to anticipate a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1 or a polynucleotide comprising the nucleotide sequence from nucleotide 12 to nucleotide 2900 of SEQ ID NO:1, as recited in independent claim 32.

Further, Nagase et al. fails to describe any polynucleotide

corresponding to the peptide fragments of KIAA0156. Thus, Nagase et al. fails to anticipate claim 19, which is directed to a polynucleotide corresponding to a tumor antigen peptide, said tumor antigen peptide being a peptide fragment of the protein which is encoded by the polynucleotide of claim 32.

Applicants respectfully submit that Nagase et al. fails to destroy the novelty of the present invention as recited in the claims. Withdrawal of the instant rejection is therefore respectfully requested.

Rejection under 35 U.S.C. § 103(a)

The Examiner rejects claims 3-5, 7-8, 19, 21, and 32-34 under 35 U.S.C. § 103(a) for allegedly being obvious over Nagase et al., in view of Campbell (*Monoclonal Antibody Technology*, Chapter 1, pages 1-32) and Sambrook et al. (*Molecular Cloning*, Chapters 3 and 12). Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

The Examiner asserts that it would be obvious to have placed the DNA of Nagase et al. in an expression plasmid to produce a protein. However, Nagase et al. merely sequenced KIAA0156, and did not show any function of KIAA0156. In other words, Nagase et al.

merely describes the genetic information of KIAA0156, but does not describe any chemical substance of KIAA0156.

On the other hand, the Inventors of the present application accomplished the present invention after suffering many labors which included establishing a CTL cell line from lymphocytes of a patient with esophageal cancer (KE-4CTL; deposit number FERM BP-5954), repeatedly conducting screening for a tumor antigen protein recognized by the CTL cell line, and isolating and identifying an intended protein (see Example 1). As a result of their labors, the present Inventors discovered for the first time that SART-3 could act as a tumor antigen protein (see Example 2), and that peptide fragments of SART-3 could act as a tumor antigen peptide (see Examples 4-8). Without this discovery, a new vaccine therapy using SART-3 would not have been developed.

At the time the present invention was invented, SART-3 was not known in the art to be a tumor antigen protein. Thus, there would not be any motivation to utilize SART-3 in the treatment of cancer, nor to prepare a tumor antigen peptide from SART-3. Accordingly, those skilled in the art would not readily accomplish the present invention.

For these reasons, the invention of claims 7-8, 19, 21, and 32-33 is not obvious over the cited prior art references, and

therefore dependent claims 3-5 and 34 are also not obvious. Withdrawal of the instant rejection is therefore respectfully requested.

Conclusion

Applicants respectfully submit that the above amendments and/or remarks fully address and overcome the rejections and objections of record. The instant claims are now in condition for allowance. Early and favorable action by the Examiner is respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a two (2) month extension of time for filing a reply in connection with the present application, and the required fee of $410.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any

overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachment: Version with Markings Showing Changes Made
Exhibit 1: Miyagi et al., *Clinical Cancer Research*, 7:3950-3962 (2001)

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

Please amend the paragraph on page 21, lines 23-25 as follows:

--In addition, any peptide sequence expected to be capable of binding to HLA antigens may be searched on internet using a software of NIH BIMAS [(http://bimas.dcrt.nih.gov/molbio/hla_bind/)].--

Please amend the paragraph on page 24, line 18 to page 25, line 6, as follows:

--As described above, it is known that the sequences of tumor antigen peptides that are bound to and presented on HLA-A24 obey a certain rule (motif), and in particular, the motif is that, in a sequence of a peptide consisting of 8 to 11 amino acids, the amino acid at position 2 is tyrosine, phenylalanine, methionine, or tryptophan, and the amino acid at the C-terminus is phenylalanine, leucine, isoleucine, tryptophan, or methionine (*J. Immunol.*, 152:3913, 1994; *Immunogenetics*, 41:p178, 1995; *J. Immunol.*, 155:p4307, 1994). Likewise, a similar rule (motif) can be found in the sequences of tumor antigen peptides that are bound to and presented on HLA-A2, and in particular, the motifs shown in the above Table 1 are known (*Immunogenetics*, 41, p178, 1995; *J.*

Immunol., 155:p4749, 1995). As shown above, sequences expected to be capable of binding to HLA antigens may be further searched on internet using NIH BIMAS software [(http://bimas.dcrt. nih.gov/molbio/ hla_bind/)].--

Please amend the paragraph on page 29, lines 1-10 as follows:

--As described above, the sequence rules (motifs) for peptides that are bound to and presented on HLA types such as HLA-A1, -A0201, -A0204, -A0205, -A0206, -A0207, -A11, -A24, -A31, -A6801, -B7, -B8, -B2705, -B37, -Cw0401, and -Cw0602 have been elucidated. As shown above, peptide sequences expected to be capable of binding to HLA antigens may be further searched on internet [(http://bimas.dcrt.nih. gov/molbio/ hla_bind/)]. Consequently, tumor antigen peptide derivatives containing the alteration of the amino acids in a tumor antigen peptide of the present invention can be prepared on the basis of such motifs.--

Please amend the paragraph on page 29, lines 11 to page 30, line 13, as follows:

--For example, regarding the motif for antigen peptides that are bound to and presented on HLA-A24, it is known as described above that in the sequence of a peptide consisting of 8 to 11 amino

acids, the amino acid at position 2 is tyrosine, phenylalanine, methionine, or tryptophan, and the amino acid at the C-terminus is phenylalanine, leucine, isoleucine, tryptophan, or methionine (*J. Immunol.*, 152:3913, 1994; *Immunogenetics*, 41:178, 1995; *J. Immunol.*, 155:4307, 1994). Likewise, the motifs shown in the above Table 1 are known for HLA-A2. In addition, peptide sequences expected to be capable of binding to HLA antigens is laid open on internet [(http://bimas.dcrt.nih.gov/ molbio/ hla_bind/)], and amino acid residues having properties similar to those of amino acids according to the motifs may also be possible. Accordingly, examples of tumor antigen peptide derivatives of the present invention include those peptide derivatives that comprise all or part of an amino acid sequence of the tumor antigen peptide of the present invention in which one or more amino acid residues at any positions that may be allowed for substitution according to the motifs (for HLA-A24 and HLA-A2, position 2 and the C-terminus) are substituted by other amino acids (preferably, which is the amino acid expected to be capable of binding to the antigens according to the above internet), and which derivatives have activity of binding to HLA antigens and being recognized by CTLs. Preferred examples are those tumor antigen peptide derivatives that comprise all or part of an amino acid sequence in which amino acid residues to be

substituted are selected from those at said positions according to the above motifs, and which derivatives have the above activity. A preferred length of "all or part" of an amino acid sequence is about 8 to 14 amino acids, although it may be a length of 14 or more amino acids for HLA-DR, -DP, and -DQ.--

Please amend the paragraph on page 66, lines 5-12, as follows:

--On the basis of the amino acid sequence of tumor antigen protein SART-3 shown in SEQ ID NO: 2, peptide sequences consisting of nine or ten amino acid residues that were expected to be capable of binding to HLA-A0201 were searched on internet using a software of NIH BIMAS [(http://bimas.dcrt.nih.gov/molbio/hla_bind/)]. Those examples of the searched peptides are shown in SEQ ID NOs: 25-52. These peptides were synthesized at Biologica Co. by the Fmoc method.--

In the claims:

Claims 19, 32, and 33 are amended as follows:

19. (Three Times Amended) An isolated polynucleotide [nucleic acid] corresponding to a tumor antigen peptide, said tumor antigen peptide being a peptide fragment of

(i) the protein which is encoded by the polynucleotide of

claim 32, or

(ii) the protein which is produced by the process of claim 5, [and]

wherein said tumor antigen peptide binds to an HLA antigen and is [being] recognized by cytotoxic T lymphocytes.

32. (Twice Amended) An isolated polynucleotide selected from the group consisting of:

(a) [a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:2,

(b)] a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1, and

(b) a polynucleotide comprising the nucleotide sequence from nucleotide 12 to nucleotide 2900 of SEQ ID NO:1 [(c) a polynucleotide which hybridizes with a polynucleotide of any one of (a) to (b), under stringent hybridization conditions comprising 6xSSC, 50% formamide, and 0.5% SDS and a temperature of 42°C],

wherein said polynucleotide of (a) and (b) encodes a tumor antigen protein which gives rise to tumor antigen peptide(s) that bind(s) to an HLA antigen and are recognized by cytotoxic T lymphocytes.

33. (Amended) An isolated recombinant polynucleotide [nucleic acid] comprising [at least one of] the polynucleotide [nucleic acids] of claim 19.